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MESCAL BUTTONS

**ANHALONIUM LEWINII—Hennings (LOPHO-
PHORA WILLIAMSII LEWINII—Coulter)**

BY

D. W. PRENTISS, A.M., M.D.

Professor of Materia Medica and Therapeutics, Medical Department
of Columbian University

AND

FRANCIS P. MORGAN, A.B., M.D.

Professor of Pharmacology, Medical Department of Columbian Uni-
versity, Washington, D. C.

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MESCAL BUTTONS.¹

ANHALONIUM LEWINII — HENNINGS (LOPHOPHORA
WILLIAMSI LEWINII—COULTER).

By D. W. PRENTISS, A.M., M.D.,

PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS, MEDICAL DEPARTMENT
OF COLUMBIAN UNIVERSITY.

AND

FRANCIS P. MORGAN, A.B., M.D.,

PROFESSOR OF PHARMACOLOGY, MEDICAL DEPARTMENT OF COLUMBIAN UNI-
VERSITY, WASHINGTON, D. C.

THE study of *Anhalonium Lewinii* is of comparatively recent date, the subject having been brought to the attention of the medical world in 1888 by Dr. Lewin, of Berlin, who published at that time the results of his observations upon the drug. In 1894 Drs. Lewin and Heffter, of Germany, reported the results of further study of the subject. In 1891 James Mooney, of the United States bureau of ethnology, in a paper read before the Anthropological Society of Washington, first brought to public attention the remarkable religious ceremonial use of the plant by the Kiowas and other tribes of the Southern plains, among whom he had been conducting researches for some time. In 1894 he brought back to Washington for examination a large quantity of mescal, under the belief that investigation would corroborate the claim of the Indians as to its valuable medicinal properties. This was given over to Mr. E. E. Ewell, of the department of agriculture for chemical analysis, and to the writers for therapeutic test. Our study of the subject has shown that the mescal buttons possess properties which are

¹ Read before the Association of American Physicians, Washington, D. C., May 2, 1896.

remarkable, the exact likeness of which is not found in any other known drug, and also that it possesses virtues which, when applied in the treatment of certain diseased conditions, may prove the drug a valuable addition to our present list of therapeutic agents. It is for these reasons that we have chosen to present this subject in this paper for your consideration.

Anhalonium Lewinii is a plant belonging to the natural order of Cactaceæ or cacti, as they are commonly called. One of the divisions of this great order is the genus *Anhalonium*, of which there are several species, and among them *Anhalonium Williamsii*, and the one now under consideration, *Anhalonium Lewinii*.

As to the exact place in botanical classification which the *Anhalonium Lewinii* should occupy, there is some difference of opinion among botanists. Hennings,¹ who first published an accurate description of the plant, believed it to be a separate species of the genus *Anhalonium*. Dr. A. Heffter² holds the same view, reasoning both from botanical characteristics and the dissimilarity in physiological action between the *Anhalonium Williamsii* and *Anhalonium Lewinii*. On the other hand, botanists who have investigated the subject more recently hold that the *Anhalonium Lewinii* is but a variety of the species *Anhalonium Williamsii*. Coulter, an authority upon the cacti, holds this view and gives the plant the name *Lophophora Williamsii Lewinii*.³ The botanist in charge of the United States botanical gardens in Washington believes that the two plants belong to the same species.

The *Anhalonium Lewinii* inhabits portions of the valleys of the Rio Grande and Pecos rivers in Texas and New Mexico, growing in barren, rocky soil, and

¹ Therapeutic Gazette, 1888.

² "Ueber Pellote." Arch. f. exper. Path. u. Phar., 1894, xxxiv., 65.

³ J. M. Coulter: "Preliminary Revision of Cacti." Bulletin U. S. Depart. Agriculture, Washington, 1894.

often in places which can be reached only with difficulty by those who gather it. It reaches a height of about one inch above the surface of the ground. The body (Fig. 1) is comparatively thick, and is surmounted by a top, which is composed mainly of the



FIG. 1.

blunt leaves of the plant. In the centre of this top is a tuft about one-half to one inch in diameter, composed of yellowish-white filaments or hairs. These tops, when dried, constitute the mescal buttons, the commercial form of *Anhalonium Lewinii*.

The mescal buttons (Fig. 2) are of a brown color,

circular, about one-half to one and a half inches in diameter and one-fourth of an inch in thickness. The edge curls upward, giving to the under surface a con-

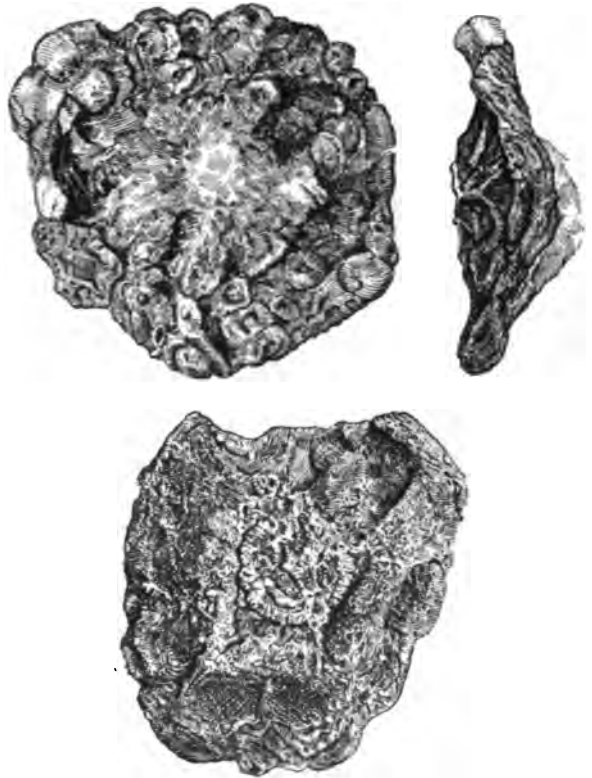


FIG. 2.

vex appearance. In the centre of the upper surface is a tuft composed of the yellowish-white hairs before mentioned, and matted down so as just about to reach the level of the upturned edge. The buttons vary in

weight from about one to eight grams, the average being about four grams.

The button is somewhat brittle and hard and can be pulverized in a mortar with difficulty. In the mouth, however, under the action of the saliva, it swells and rapidly becomes soft, the consistency which it acquires giving somewhat the sensation imparted by slippery elm. The taste is disagreeable and nauseous and very bitter, with a persistent after-taste. A marked sensation of stinging or tingling is produced in the fauces, which remains for some time after the drug has been swallowed. The powdered drug is odorless when dry, but acquires a nauseous odor upon being moistened.¹

Physiological Action.—In connection with the physiological action of the mescal, its use by the Indians is of great interest. The Kiowa Indians and their associated tribes, formerly ranging from the Arkansas River southward into Mexico, have, from the earliest period, made its use a regular part of their religious ceremonies. When finally gathered upon the Kiowa reservation in Oklahoma, which they now occupy, they continued the use of the buttons in their ceremonies, the demand being supplied by traders who obtain it from the valley of the Rio Grande. Its use has spread to such an extent that the rite has become the chief religion of all the tribes of the Southern plains. Complaint being made to the government authorities at Washington by missionaries and others, the eating of the drug was rendered unlawful and was forbidden under severe penalties. Nevertheless, the use of the mescal has persisted to the present time.

The religious ceremony, as described by Mr. Mooney, who has participated in it several times, usually takes place on Saturday night. The men seat themselves in a circle within the tent, around a large

¹ The writers, in *Therapeutic Gazette*, September, 1895.

fire which is kept burning brightly. After a prayer the leader hands each man four buttons, and each, having been freed from the tuft of hairs, is put into the mouth and, after it is thoroughly softened, is ejected into the palm of the hand, rolled into a bolus, and swallowed. At midnight each man calls for as many mescals as he wants, and in this way ten or twelve of the buttons, as a rule, are taken at intervals between sundown and daybreak. They sit quietly throughout the ceremony, while the fire is kept burning brightly and a continual singing and beating upon the drum is kept up. Most of the time they are in a state of reverie, the intoxication of the drug showing itself in the visions of color and other manifestations which will be described later. The hours are interspersed with songs, prayers for the sick, and baptismal rites. They sit thus from sundown to nearly noon of the next day. At the close of the ceremony they go out, it is claimed, without the slightest depression or unpleasant after-effect. Upon the day following the ceremony they carefully abstain from the use of common salt with their food; this, it seems, for a religious reason, and not because of any incompatibility of salt with the drug or its effects.¹

To determine the physiological action of the crude drug — the mescal buttons themselves — upon the human system, they were administered in varying quantity to different young men who kindly volunteered their services for the purpose. Eight of these experiments were made, and in each enough of the drug was given to produce decided characteristic symptoms. Observations were taken at frequent and regular intervals to ascertain the effects upon the different portions of the body. Most of these experiments have been reported in full,² but time does not permit

¹ See also "Mescal Plant and Ceremony," James Mooney, *Therapeutic Gazette*.

² *Therapeutic Gazette*, September, 1895.

us to give a detailed account of them. The following are briefly the results obtained:

The most remarkable of the physiological effects of the drug was the production of visions. These appeared in most cases after three of the buttons had been taken. The visions ranged from ill-defined flashes of color to most beautiful figures, forms, landscapes—in fact there seemed to be absolutely no limit to the variety of visions which the drug could produce. They could in but few cases be seen with the eyes open, but upon closing them an ever-changing panorama appeared. Drumming, or otherwise marking regular time, had a marked effect upon the visions—much enhancing the beauty and variety of the objects seen. The fact is of interest in connection with Mr. Mooney's statement that during the eating of the mescal by the Indians there is kept up a continual beating upon the drum. In three cases the visions were under the control of the will, and in two they were subject to the suggestion of others. The effect of the drug in the production of visions is probably due to stimulation of the centres of vision in the brain. The persistent ache and feeling of exhaustion in the occipital region, which persisted for several days after one of the experiments, is of interest in this connection.

A clearer idea of the nature of these visions is given by the following extract from one of the cases already reported. In all other cases, similar effects were produced. "The first sensations that followed my taking the drug came upon thoughtlessly closing my eyes. Instantly there sprang into the field of view a host of little tubes of shining light, down which green and red balls the size of peas were constantly rolling. The tubes of light bent themselves into the shape of letters, but they would spell nothing, and, slowly curving themselves into grotesque shapes, began to revolve rapidly, the green and red balls going in the opposite

direction with even greater velocity. All the field of view between these silent wheels was filled in with a shifting mass of green. The colors were wonderful. They were the colors of the spectrum intensified as though bathed in the fiercest sunlight. No words can give an idea of their intensity or of their ceaseless, persistent motion. The figures constantly changed in form and color, but always remained a series of fantastic curves, revolving rapidly back and forth upon their own axis. The forms changed through rich arabesques, Syrian-carpet patterns, and plain geometric figures, and with each new form came a new flush of color, every shade appearing, from pure white to deepest purple. When the eyes opened and the light was turned up, the visions faded like stars going out in daylight, and the room, tables, chairs, and all surroundings came back into real existence and within reach of the hands."

It will be seen that the predominating hallucinations are the wonderful color phenomena, although the figures, forms, etc., are in themselves sources of pleasure and admiration.

In some cases no effect whatever was produced upon the reason or will of the individual. In others, there was some slowness of thought and loss of power of expression, and in one of the experiments a marked delusion. Compared with other drugs of this class, however, the effect upon the mind is extremely slight.

Dilatation of the pupil was well marked in every case, and persisted for from twelve to twenty-four hours after the drug was taken. The dilatation was accompanied by a slight loss of the power of accommodation and consequent disturbance of vision.

More or less depression of the muscular system existed in every case, and this was the first effect noticed after the drug was taken. It ranged from a feeling of lazy contentment to marked muscular depression. Susceptibility to this effect varied widely. Whether

the sedative effect is produced by action on the nerve centres, peripheral nerves, or their nerve endings, or on the muscular fibres themselves is not yet determined, but indications point to action through the nerve centres.

Partial anæsthesia of the skin was present in three of the cases, appearing when the effects of the drug began to wear off.

The heart action is at first rendered slower and stronger. This is followed by a rise to the normal, which continues during the period of greatest activity of the drug. In the cases in which the muscular depression was greatest, slight if any depression of the heart was present.

The respiration was unaffected in all cases but one. In this it seemed to partake slightly of the general muscular depression.

Upon the stomach the drug produced an effect which varied from a feeling of uneasiness and fulness at intervals, to nausea and vomiting.

Inability to sleep for at least twelve hours after the influence of the drug passed off was a uniform effect.

Appreciation of the duration of time was lost in all cases—as in the effect of *cannabis indica*. In one case a snowstorm appeared to last an hour, although in fact the vision continued not more than one minute.

No constant effect upon the bowels, skin, temperature, or secretion of the various glands of the body was found.¹

The only record of the taking of *Anhalonium Lewinii* for experimental purposes which we have been able to find is that of Briggs.² He took “a third of a specimen,” and the symptoms produced were the following: In fifteen minutes the pulse rose from 60 to 70. In thirty minutes there was fulness of the head, pulse 90,

¹ Therapeutic Gazette, September, 1895.

² Lewin: Archiv für experimentelle Pathologie und Pharmacologie, Band xxxiv., Heft 5 u. 6.



respiration 26. The sense of fulness increased, and was followed by a headache and swimming in the head. Suddenly the pulse shot up to 160, and the respiration increased so that he could with difficulty get sufficient breath to keep himself alive. He thought he was about to die, and became unconscious. In six to eight hours his pulse and respiration went down again to the normal. Great depression existed for twelve hours.

The symptoms produced in this experiment are so widely different from those which we have obtained from administration of the drug that we cannot believe that the drug taken by Briggs was the same one which we have now under consideration.

Lewin,¹ in experiments upon animals, found that in them the drug produced an acute muscular spasm of varying intensity, with increased reflexes, its action in this particular much resembling that of strychnine or brucine. No such effect was present, however, in our experiments upon man. Whether or not it would be produced by much larger doses is, of course, a matter of conjecture. In some animals, also, a quickened respiration was noted, which effect was present in our experiments only in one case, and in the presence of great general muscular depression. In animals, also, the heart remained unaffected, whereas in man we found a primary slowing of the heart action. In both animals and man more or less tendency to nausea and vomiting existed in most cases.

The physiological action of Anhalonium Lewinii upon man cannot be said to be identical with that of any other known drug. Its effects resemble those of certain drugs in some of the symptoms produced, but differ widely from them in others. Cannabis indica produces visions, with dilated pupils and with slight effect upon the circulation. In these particulars its ac-

¹ Archiv für experimentelle Pathologie und Pharmakologie, Band xxxiv., Heft 5 u. 6.

tion is similar to that of Anhalonium Lewinii. But Cannabis indica is a hypnotic, and the delirium and hallucinations are in most cases followed by sleep. Anhalonium Lewinii, on the other hand, tends to produce wakefulness in every case. The Indians do not sleep for twenty-four hours after the commencement of their ceremony, and in our experiments sleep was found to be impossible for about the same length of time.

In this tendency to produce wakefulness it resembles cocaine. The visions produced by Cannabis indica "are generally of a gay character, producing much merriment, accompanied by a great inclination to muscular movement."¹ The visions of Anhalonium Lewinii provoked wonder and admiration, but no merriment, and there was present disinclination to make any muscular effort. Other marked differences exist, which will become evident to any one comparing the action of the two drugs.²

Alkaloids of Anhalonium Lewinii.—In 1888 Lewin subjected the mescal buttons to analysis and succeeded, by chemical methods which need not be given here, in obtaining an alkaloidal substance, to which he gave the name anhalonine, and to which he ascribed the chemical formula $C_{11}H_{11}NO_3$. Mr. Ewell,³ who has succeeded in obtaining anhalonine in a pure state, describes it as a white strongly alkaline substance. It crystallizes from aqueous solution in prismatic, sometimes tabular crystals of the rhombic system. It is soluble in a large quantity of water, and is unusually soluble in alcohol, ether, chloroform, benzin, and petroleum ether. Its melting-point is

¹ Brunton: "Pharmacology, Materia Medica, and Therapeutics," p. 1,026.

² The writer, in Therapeutic Gazette, September, 1895.

³ I am indebted to Mr. E. E. Ewell, Bureau of Chemistry, U. S. Department of Agriculture, for the chemical description of the constituents of mescal buttons and the photographs reproduced in this article.

77.5° C., and it can be sublimed without decomposition. It forms salts with the ordinary acids.

Anhalonine hydrochlorate (Fig. 3), which was used in our experiments with the first alkaloid, is a white, odorless substance forming needle-like crystals. It is soluble in water in the proportion of two parts per



FIG. 3.

one hundred. The solution is very bitter to the taste. The hydrochlorate is also soluble in alcohol. It melts at 254°-255° C. with decomposition. It rotates the plane of polarized light to the left. Lewin describes an amorphous as well as a crystalline hydrochlorate, but Mr. Ewell believes that the former is but an impure hydrochlorate.

Lewin¹ describes anhalonine sulphate as forming needle-like crystals, colorless or of a slightly yellowish tinge; easily soluble in cold water, but much more so in hot water; almost insoluble in alcohol and ether.

The physiological action of anhalonine upon guinea-pigs and other small animals has been investigated by Lewin and Heffter. Lewin found that in these animals the alkaloid produced at first a primary collapsed condition, which was followed by an increase in the reflex excitability, and, if the dose administered was large enough, convulsions which resembled to a certain extent those produced by strychnine. The action of the drug, so far as these experiments would indicate, is somewhat analogous to that of strychnine. The lethal dose was found to be 0.16 to 0.20 gram per kilogram of body weight.

These results we have verified by a series of experiments upon guinea-pigs in the laboratory. The following experiment is fairly typical.

Guinea-pig; weight, four hundred and twenty-five grams.

1:01. Injected 0.05 gram anhalonine hydrochlorate in solution.

1:03. Tremor of body.

1:05. Tremor of body. Opisthotonos, followed by convulsion.

1:08. Slight convulsion. Pulls itself around by front legs; hind seem paralyzed. Opisthotonos.

1:10. Convulsion on touch.

1:12. Breathing rapid. Tremor of front extremities.

1:15. Attempts to move but cannot, except extremities.

1:25 to 1:40. Constant convulsive movements of whole body. Normal reflex to touch, breath-of-air sound, etc., exaggerated.

1:30. Biting and chewing. Opisthotonos.

¹ Archiv f. exper. Path. u. Phar., 1888, xxiv., 401.

1:40. On feet. Condition better. No tremor or convulsions.

1:45. Convulsion, precipitated by rubbing back. After it, legs extended for a short time.

1:47. Sits up. From this time gradually improved.

In order to ascertain the action of anhalonine upon man, Dr. Morgan took the drug in progressively increasing doses daily up to 0.20 gram without any appreciable effect. As this amount is nearly four times



FIG. 4.—Third Alkaloid. $\times 9$ diameter.

the quantity of anhalonine contained in the crude drug administered in the experiment already reported, it is evident that anhalonine cannot be the active principle of mescal buttons, or even a potent factor in the production of their effects. A second alkaloid has also been obtained from Anhalonium Lewinii,¹ and

was called by Heffter alkaloid B. This, for convenience, we shall call mescaline. Its formula, crystalline form, solubility, etc., are now being made a subject of study by Mr. Ewell. It is soluble in ether, chloroform, and petroleum ether. In the last it is much more sparingly soluble than is anhalonine. It forms a hydrochlorate with hydrochloric acid.

Mescaline hydrochlorate is a white substance, forming tabular crystals. It is much more soluble in water and alcohol than is anhalonine hydrochlorate.

We have conducted a series of experiments upon guinea-pigs to determine as nearly as possible the

¹ Dr A. Heffter: Arch. f. exper. Path. u. Phar., 1894, xxxiv., 66.

characteristic effects of mescaline, and in what particulars its action differs from that of anhalonine.

I.—Guinea-pig; weight, five hundred and seventy-six grams; 0.01 gram mescaline hydrochlorate in solution, hypodermically. No appreciable effect. Later, 0.02 gram injected in same animal. No decided effect. Seemed more sluggish in movement and less easily frightened than normally. Breathing more rapid.

II.—Guinea-pig; weight, four hundred and twenty-five grams.

12:15 P.M. 0.03 gram mescaline hydrochlorate, hypodermically into inner side of thigh.

12:19. In corner. Apparently drowsy. Will not move when struck.

12:23. Tremor of head and body.

12:28. Most rapid convulsive movements of extremities, as if running, but makes little progress, as feet seem to take no hold upon floor.

12:30. Quiet, on belly, in natural position.

12:43. Same; seems drowsy. Recovery from this time.

III.—Guinea-pig; weight, four hundred and sixteen grams.

12:53. 0.04 gram mescaline hydrochlorate in solution, hypodermically.

12:57. Runs around uneasily. Rapid chewing-movements of jaw.

12:58. Pupil slightly dilated. Chews rapidly. Tremor of head.

12:59. Runs around in frightened manner, with tremor of body. Chews. Breathing rapid.

1:00. Runs around, jumps high, and falls on side in convulsion. Extremities stiff. Opisthotonos.

1:01. On feet again. Tremor. Breathing rapid.

1:02. Pupil dilated. Breathing rapid and labored.

1:05. Violent convulsion.

1:06. More quiet. Tremor.

1:11. Looks around more normally. Breathing 150 per minute and difficult. Whole body shakes.

1:16. Moves backward. Breathing same.

1:20. Breathing 120 per minute. Walks backward.

1:33. Runs backward around cage.

1:40. Breathing 104, but more irregular.

2:10. Walks backward. Breathing much slower, but weak and irregular.

3:00. Animal bright and runs forward when touched suddenly. Recovery.

IV.—Guinea-pig.

1:00. 0.047 gram mescaline hydrochlorate in solution, hypodermically.

1:03. Frightened and restless. Breathing rapid.

1:04. Rapid chewing-movement at intervals.

1:05. Very restless. Tremor on moving. Respiration irregular and labored.

1:06. Cries out. Runs around at intervals.

1:08. Jumps up and falls on side in convulsion. Extremities rigid.

1:08 ½. Gasping on side.

1:10. Respiration ceased.

1:13. Thorax and abdomen opened. Auricles and ventricles found beating, but not synchronously. Auricles beating rhythmically at 60 per minute. Ventricles, 26 per minute.

1:27. Ventricles 24 per minute and very weak. Two drops ten-per-cent. solution mescaline hydrochlorate dropped upon heart. Beats become more rapid and stronger than before, and continue so for several minutes.

1:38. Ventricles, 42 per minutes.

1:47. Heart ceases to beat thirty-seven minutes after breathing ceased. Cavities dilated and filled with dark blood. Pupils dilated to maximum extent. Lethal dose in this experiment, 0.12 per kilogram of body weight of animal.

V.—Guinea-pig; weight, three hundred and eight grams.

12:09. 0.054 gram mescaline hydrochlorate in solution, hypodermically.

12:10. Tremor of body. Increased restlessness. Runs around.

12:11. Restless. Convulsion, as in last experiment.

12:13. Convulsive movements continue. Pupils dilated.

12:14. Gasping on side.

12:16. Dead. At autopsy pupils found dilated to maximum extent. Heart stopped in diastole; cavities filled with dark blood. Lethal dose in this experiment, 0.17 per kilogram.

Experiments with mescaline hydrochlorate upon kittens gave practically the same results. The pupil was dilated even by small doses. The breathing soon became very rapid and shallow. Convulsions similar to the ones above reported were produced, and the heart continued to beat after respiration had ceased. The lethal dose was found to be practically the same. The most important difference in effect was that in kittens the drug seemed to act from the very first to depress the muscular system, the animals resting throughout the experiments upon the belly, the extremities extended flat upon the table. They attempted to move around, but could not.

It is evident from these experiments that the effects of mescaline are widely different from those of anhalonine. The minimum lethal dose of mescaline in our experiments as found to be 0.12 per kilogram, whereas Lewin found the lethal dose of anhalonine to be 0.16 to 0.20 per kilogram.

While both alkaloids in large doses produce convulsions, those of mescaline are different in character from those produced by anhalonine. As already stated, the convulsions of anhalonine somewhat re-

semble those occurring in strychnine poisoning. They are accompanied by some increase in the reflex excitability and more or less opisthotonos, and they can be brought on by external stimulation. While the animal under the influence of mescaline exhibits at times great restlessness, nevertheless the effects are not accompanied by increased reflex excitability and the animal appears rather less responsive to external stimulation than normally, and convulsions cannot be precipitated by such stimulation. Opisthotonos also is not a marked feature of the full effects of the alkaloid, although it is present to a slight degree during the convulsions.

It would appear that the convulsions produced by mescaline more closely resemble those caused by non-oxygenation of the blood. The effects of the alkaloid are accompanied by rapid and difficult breathing and symptoms of respiratory embarrassment. In experiment III. this was true to such an extent that all the muscles of the body seemed to be brought into play to aid the animal in obtaining sufficient air, and the appearance presented was that of intense dyspnoea. Death also is preceded by respiratory failure, the heart continuing to beat for a variable length of time after the breathing ceases. After death the ventricles are found dilated and filled with dark blood. Furthermore, Heffter,¹ who made a limited number of experiments with this alkaloid upon frogs, makes no mention of convulsions as an effect of the drug in that class of animals; whereas in our experiments upon animals of higher development, convulsions were a constant symptom when the drug was administered in large dose. This alone would lead us to believe that the convulsions produced by mescaline are asphyxial in character and produced by contact of the non-oxygenated blood with the motor-nerve centres, it being a well-known fact that asphyxial convulsions do not

¹ Archiv f. exper. Path. u. Phar., 1894, 34, 65.

occur in frogs, whereas they do occur in animals of higher development. Brunton¹ states that if any drug produces convulsions in the higher animals and not in frogs, the probability is that the convulsions it produces are asphyxial, and not due to direct irritant effect of the drug upon the motor centres. This, taken in connection with the facts already stated, leads us to believe that the convulsions produced by mescaline are asphyxial in character.

From these experiments it is also evident that mescaline has no influence upon the heart as a depressant, even when administered in fatal doses.

When given hypodermically it acts to dilate the pupil. No effect upon the pupil was obtained by dropping a five or ten per cent. solution of the hydrochlorate into the eye.

The alkaloid appears to depress the muscular system and the respiration.

In its constitutional effects, mescaline much resembles cocaine, and the similarity in action will at once become apparent in comparison with the effects of the latter drug upon the lower animals.²

From the mother liquor left after the separation of anhalonine and mescaline, Mr. Ewell has succeeded in obtaining a third alkaloid, entirely different in its chemical and physiological properties from the two already considered. The hydrochlorate of this third alkaloid, which was the salt used in our experiments, is white or of a slightly yellowish color. It forms nodular groups of radiating needle-like crystals (Fig. 4) which are readily soluble in water and alcohol. The taste of the crystals is acrid and slightly bitter, with a persistent after-taste. Its reaction is neutral.

We have performed a series of experiments upon

¹ Pharmacology, Materia Medica, and Therapeutics," pp. 189 and 237.

² See H. C. Wood: "Therapeutics, Its Principles and Practice."

the lower animals to determine so far as possible the physiological effects of this alkaloid.

I.—Rabbit; weight nine hundred and eighty-five grams.

11:55. 0.0133 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

11:56. Restless. Great tremor. Animal rises upon four extremities, which are perfectly rigid, and pointing outward from body like the legs of a "sawhorse," and seems to be propelled slowly around table by violence of tremor.

11:57. Quiet, on belly, hind legs flat on table. On touch, extremities become rigid and violent tremor appears.

11:58. On feet, with rigid extremities and tremor as above.

11:59. Breathing rapid. Quiet if not touched. On touch, convulsive movements.

12:02. Breathing very rapid. Heart 156 per minute.

12:05. Breathing same. No convulsive movements on touch. Hind legs flat on table.

12:07. Hops fairly normally, using back legs awkwardly. Recovery from this time, breathing and heart gradually becoming slower to normal. Amount injected in this experiment, 0.0136 per kilogram of body weight.

II.—Rabbit; weight, five hundred and twelve grams.

12:07 1/2. 0.01 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

12:08. Tremor, especially of hind extremities.

12:09. Violent tremor. In hopping, hind legs somewhat stiff. Breathing rapid.

12:10 1/2. "Sawhorse" phenomenon as in last experiment lasting about ten seconds, after which, animal fell on side in tetanic convulsion. All muscles rigidly contracted. Opisthotonos, and extension of extremities. Followed by gradual relaxation of all muscles.

12:11. Muscles flaccid. Breathing ceased. Lethal dose in this experiment, 0.02 per kilogram.

III.—Rabbit; weight, one thousand one hundred and sixty-five grams.

2:19½. 0.03 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

2:21. Tremor of body.

12:21½. Tremor so violent as almost to amount to convulsive movement.

12:22. "Sawhorse" phenomenon, as in preceding experiments, after which animal fell on side. Convulsive movements. Rigid extremities. Opisthotonos.

12:22½. Gradual relaxation. Breathing found to have ceased.

12:35. Thorax opened. Heart still beating. Heart ceased in diastole, twenty-seven minutes after breathing stopped. Lethal dose in this experiment, 0.025 per kilogram.

IV.—Rabbit; weight, four hundred and seventy-six grams.

11:37. 0.025 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

11:38. Violent tremor. Jumped up and fell on side in convulsions. Opisthotonos, extremities extended, and all muscles rigid. No movement.

11:39. Convulsive twitchings. Gradual relaxation.

11:40. Breathing ceased.

11:45. Thorax opened. Heart beating rhythmically, 21 per minute.

11:50. Heart beating more slowly. Finally stopped in diastole.

Lethal dose in this experiment, 0.053 per kilogram.

In guinea-pigs the alkaloid produced effects very similar to those produced in rabbits.

V.—Guinea-pig; weight, seven hundred and eight grams.

12:29. 0.007 hydrochlorate of alkaloid 3 in solution, hypodermically.

12:31. Slight tremor of ears.

12:34. Much startled by sudden noise, as rapping table with pencil.

12:41. Same. Restless.

12:47. Quiet. Jumps clear from table when blown upon, or upon sharp noise.

12:51. Same. Cries on being touched. Runs awkwardly with violent tremor.

12:53. Increased reflex excitability continues. Not frightened by object brought rapidly toward it. Condition remained as described until 1.09 when it gradually became normal. Amount injected in this experiment, 0.01 per kilogram.

VI.—Guinea-pig; weight, seven hundred and thirteen grams.

11:45. 0.0196 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

11:46½. Slight tremor. Runs around.

11:48. Violent tremor, especially on moving.

11:50. Violent tremor. Falls on side. Muscles of body and extremities contracted and rigid. Extremities extended. Opisthotonos.

11:50½. Gradual relaxation. Hair on fore part of body "on end."

11:51 to 11:55. Alternating tetanic spasms and relaxation. Breathing absent during spasm, accelerated during intervals.

11:56½. Animal on side. Constant spasmodic twitchings of head, body, and extremities, continuing until

12:05. Heart and breathing rapid. Tetanic spasms can be precipitated by touch or irritation.

12:05½. Tetanic convulsion followed by relaxation.

12:06. Gasping. Breathing gradually becomes regular and slower.

12:09. Can stand on feet. Hair still "on end."

12:11. Moves around awkwardly. Recovery. Amount injected in this experiment, 0.0275 per kilogram.

VII.—Guinea-pig; weight, six hundred and eight grams.

12:00. 0.0182 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

12:02. Tremor on moving.

12:04. Tetanic convulsion. Extremities extended. Opisthotonos, followed by relaxation. Hair on fore part of body "on end."

12:05 to 12:10. Alternating tetanic spasms and relaxation.

12:10. Gasping. Opisthotonos.

12:12. Tremor. Spasmodic twitchings.

12:14. Same.

12:20. Heart rapid, breathing fairly normal.

12:26. Tetanic convulsion brought on by touch, followed by gradual relaxation. Breathing found to have ceased.

12:30. Thorax opened. Heart still beating.

12:50. Heart ceases. Lethal dose in this experiment, 0.03 per kilogram.

In frogs effects were produced which even more clearly indicate the physiological action of the alkaloid under consideration. These effects were similar to those produced in guinea-pigs and rabbits. A series of experiments upon frogs was made, of which the following may be considered typical:

VIII.—Frog; weight, one hundred and eighty-three grams.

2:33. 0.00549 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

2:37. Increased reflex excitability to touch.

2:39. Reflex excitability still more increased. Violent sudden extension of extremities on touch.

2:44. Tetanic convulsion on touch, or other slight irritation. Animal lies perfectly quiet; when

touched, however, tetanic convulsion appears, with contraction and rigidity of all muscles and extension of extremities, which lasts for a few seconds, followed by relaxation and quiet until again irritated.

Condition remained same for several hours, and it was dead upon following morning. Lethal dose in this experiment, 0.03 per kilogram.

IX.—Frog; weight, two hundred and sixty-eight grams.

12:02. 0.008 gram hydrochlorate of alkaloid 3 in solution, hypodermically.

12:06. Increased reflex to touch.

12:08. Reflex increased. Irritation produces sudden violent extension of extremities.

12:11. Animal quiet unless touched, when violent tetanic convulsion occurs, as in last experiment.

1:05. Spinal cord divided at about its middle. Reflex tetanic contractions persist below as well as above point of section. Lethal dose in this experiment 0.03 per kilogram.

Other experiments upon frogs were made with the same results.

From these experiments it is evident that the third alkaloid is much more powerful than either anhalonine or mescaline, and differs from them also in its physiological effects. Its lethal dose in frogs, guinea-pigs and rabbits is 0.02 to 0.03 per kilogram of body weight.

The most marked effect of the alkaloid is to increase the reflex excitability of the animal. This was produced by doses as small as 0.0136 per kilogram. As the amount given was increased, this effect became more marked, and when large doses were administered violent reflex tetanic convulsions were produced. These effects were due to action through the spinal cord, as they persisted below the point of section, after the cord had been divided and the parts severed from connection with the brain.

The similarity in action between this alkaloid and strychnine is remarkable. Experiments were performed in which a frog was given alkaloid 3 and another at the same time strychnine, and the effects of the two drugs were compared. Almost no difference in effect whatever could be distinguished, the third alkaloid producing increased reflex excitability as surely and to as marked an extent as the strychnine.

The effect of chloral hydrate upon an animal to which the alkaloid had been administered is also of interest. To ascertain this, a lethal dose of alkaloid 3 was given to one frog, and to another the same dose of alkaloid 3, and in addition chloral hydrate in varying quantity in different experiments.

X.—3:40. Frog A, 0.03 per kilogram hydrochlorate of alkaloid 3 in solution, hypodermically.

Frog B, same, and in addition chloral hydrate, 1.00 per kilogram, in solution, hypodermically.

In frog A increased reflex excitability was noted in four minutes. The effect deepened into reflex convulsions upon irritation, as in experiments already reported, which continued until the death of the animal.

Frog B appeared normal at 3:45 and 4:00.

4:05. Extremities appear weak, and animal rests upon belly. By no stimulation can any increased reflex excitability be demonstrated.

4:07. Same. Stupid. No increased reflex. Condition remained same until death at 4:20, apparently from the effects of chloral. At no time did any increase in reflex excitability appear.

Other similar experiments were made in which, the dose of the third alkaloid remaining the same (0.03 per kilogram), the amount of chloral administered was progressively lowered. It was found that no increase in reflex excitability appeared until the amount of chloral was lowered nearly to 0.25 per kilogram. As the amount was still further lowered, reflex tetanic

convulsions and the typical effects of the alkaloid appeared.

Furthermore, chloral appeared to act in frogs as an antidote in poisoning by the drug.

XI.—Frog; weight, three hundred and forty-four grams.

11:30. Injected lethal dose of hydrochlorate of alkaloid 3, 0.0103 in solution (0.03 per kilogram); also 0.086 of chloral hydrate (0.25 per kilogram).

11:37. Slight increase of reflex excitability to touch.

11:48. Same, more marked. Extension of legs on touch. Draws them up, however, and stands normally.

11:53. Tetanic convulsion on touch. Stupid. Rests on belly. Tries to hop occasionally. Draws legs up normally. Condition remained same for several hours and recovery upon following morning was complete.

XII.—In this experiment the same lethal dose (0.03 per kilogram) was injected, and but 0.125 of chloral hydrate per kilogram. Animal recovered.

In these experiments the amount of chloral given was insufficient entirely to counteract the effect of the alkaloid, but the animals recovered from what would otherwise have been a fatal dose of the third alkaloid.

From the results of these experiments we conclude that the most marked physiological effect of the third alkaloid of mescal buttons is the production of increased reflex excitability, and, if the amount given be sufficiently large, reflex tetanic convulsions; this effect is produced by action through the spinal cord; chloral hydrate directly antagonizes this effect of the alkaloid, in small doses modifying the increase in reflex excitability, and in sufficiently large doses counteracting it entirely; and that the symptoms produced by the alkaloid in frogs, guinea-pigs, and rabbits appear to be identical with those produced by strychnine.

The action of the alkaloid upon the respiration and

heart appeared to be entirely secondary to its effect upon the muscular system and the degree of involvement of the muscles of respiration. The breathing was absent during the tetanic convulsions and more rapid than normal during the interval of quiet, as was also the heart. No marked effect upon the pupil was found.

Other Constituents.—In addition to alkaloids, mescal buttons contain other ingredients, the most important of which is a resinous substance, which may be found to play an important part as the active principle of the drug. It is soluble in alcohol and ether, insoluble in water, and seems to be of a complex nature, as it can be separated into two or more portions by proper solvents. The buttons also contain other substances which possess more of chemical than of pharmacological interest. These include one or more wax-like bodies, and some of the carbohydrate constituents of the plant.

Therapeutic Uses.—The conditions in which it seems probable that the use of mescal buttons will produce beneficial results are the following: In general "nervousness," nervous headache, nervous irritative cough, abdominal pain due to colic or griping of the intestines, hysterical manifestations, and in other similar affections in which an antispasmodic is indicated; as a cerebral stimulant in neurasthenia and in depressed conditions of the mind—hypochondriasis, melancholia, and allied conditions; as a substitute for opium and chloral in conditions of great nervous irritability or restlessness, in active delirium and mania, and in insomnia caused by pain. In the last condition it acts to produce sleep not as a hypnotic, but by relieving the cause of the insomnia. In full physiological doses it produces insomnia, but in therapeutic doses it does not have this effect.

The following cases in which the drug was used may be mentioned briefly:

I.—Gentleman, aged fifty-five years. Chronic bronchitis with asthmatic attacks. Much distressed by an irritative cough which kept him from sleeping. A piece the size of a pea from the centre of a button was administered in the afternoon, to be dissolved slowly in the mouth. The irritative cough was speedily relieved. He took a second similar dose at bedtime and slept well through the night, which he had not done before for a long time. He returned to his home in New York and kept up the use of the drug with continued relief. In a letter received from him recently he states that he has improved very much, being able to sleep all night without rising, which he had not been able to do for two years; and that, although he has no need of it upon some days, he carries a piece of a button in his pocket constantly, as its use relieves the tickling in his throat at once and gives greater relief than any other remedy which he has ever used. It appears to have no curative effect—merely relieves the irritative cough.

II.—Gentleman, principal of high school, aged twenty-five years. Neurasthenia of six months' standing. The effect of the drug in this case seemed little less than marvellous. Three buttons were administered within an hour. This was followed by the characteristic color visions of the drug, and relief from the bodily and mental fatigue with which he had suffered for six months, and he declared that he was "himself again, cheerful and happy." On the next day, and for several days thereafter, he continued to feel the beneficial effects of the drug. He has continued its use in dose of one-half a button when he feels it to be necessary. It invariably relieves the sense of bodily and mental fatigue.

III.—Lady, aged thirty-three years. Nervous prostration. The drug was administered in this case as in the last, but in smaller doses, with a marked beneficial effect. Mental and physical exhaustion were re-

lieved and power to work was increased to a marked degree. There was no reaction.

IV.—Lady, aged forty-nine years. Chronic phthisis with facial neuralgia and catarrh of pharynx, larynx, and bronchi. The fluid extract of anhalonium was administered with beneficial effect. The irritative cough was relieved to a marked extent, the spells of coughing being less frequent and less violent and prolonged. Although she has been taking the drug but a comparatively short time, she has suffered much less than formerly from the facial neuralgia.

The following cases were reported by a gentleman of a Western State. The drug was administered under the supervision of his family physician:

V.—Gentleman, aged fifty-six years, large and strong physically. "Softening of the brain," onset dating back about a year. He was under the care of his two brothers who were physicians in Kansas, and was at times violent and required the constant attendance of a physician and two nurses. In an attack of violence, opium in the form of laudanum and morphine was given, commencing on Thursday, until the following Sunday, without beneficial effect. Upon Sunday at 2 P.M. he was given a teaspoonful of tincture of anhalonium. A teaspoonful was also given every half hour from 6 until 9 P.M. At 10:30 the patient went to sleep and awoke at seven o'clock, Monday, in rational condition. He felt so much improved that he left the next day for his home in Texas. The course of the original disease was not influenced by the drug, and he died a few months later.

VI.—Sister of above-mentioned gentleman reporting cases. "Very low and out of her head." One of the physicians above referred to used chloral to quiet her, and, this failing, administered tincture of anhalonium. It quieted her in a few minutes and she slept well and long. It seemed to be the turning-point in her illness, as she fully recovered.

The same gentleman reports that his wife formerly used to take the tincture for nervous headaches and that it always relieved her. She has them so seldom now that she does not use it.

The following preparations are suggested: *Extractum anhalonii fluidum* (one hundred per cent.). Dose, one-half to one gram (ten to fifteen drops).

Tinctura anhalonii (ten per cent.). Dose, four to eight grams (one to two teaspoonfuls).

Anhalonium (in form of buttons or powder). Dose, one-half to one gram (seven to fifteen grains).

The tincture should be made by the process prescribed in the United States Pharmacopœia for the preparation of tinctures. It should be of ten-per-cent. strength. The fluid extract should be made of one-hundred-per-cent. strength and in accordance with the method prescribed in the United States Pharmacopœia for the preparation of fluid extracts.

The taste of these liquid preparations is very bitter, but may be disguised by a suitable vehicle, such as a mixture of fluid extract of licorice and elixir of yerba santa.

In conclusion we would say that *Anhalonium Lewinii* (mescal buttons) must not be confounded with the intoxicating drink "mescal," used by the Mexicans and others. This drink is the fermented juice of one or more of the species of agave.

1230 NINTH STREET, N. W.

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